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EXAMINER
SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
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16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/629,469	Applicant(s) OTA ET AL.	
	Examiner Carolyn L Smith	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-35* is/are pending in the application.

4a) Of the above claim(s) *1, 6-7, 9-10, 14, 16-17, 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *24-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Sequence Match Listing (1 page).

DETAILED ACTION

Applicants' election without traverse of Group II (claims 2-5, 8, 11-13, 15, and 18) and sequence election of SEQ ID NO: 10847; the further sequence election of SEQ ID NO: 702, 6233, and 10848; the cancellation of claims 2-5, 8, 11-13, 15, and 18; and the addition of new claims 24-35 in Paper No. 14, filed 1/21/03, is acknowledged. Claims 1, 6-7, 9-10, 14, 16-17, and 19-23 are withdrawn from consideration as being drawn to non-elected Groups.

The corrected drawings, filed 1/21/03, have been approved by the draftsman.

The information disclosure statement filed 12/26/01 fails to comply with the provisions of 37 CFR 1.97, 1.98, and MPEP § 609, because the reference by Maruyama et al. is in a foreign language. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609, ¶ C(1).

Claims herein under examination are 24-35.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 2, lines 30-32 and elsewhere. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

PATENTABLE UTILITY GUIDELINES

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

Claims Rejected Under 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24-35 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The critical limitation of claims 24-35 are the nucleotide sequences of the claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides

involving sequences of SEQ ID NO: 702, 6223, 10847, and 10848. The claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides are not supported by a specific utility, because the disclosed uses of these compositions are not specific and are generally applicable to the polynucleotide. The specification states "full-length CDNA provides valuable information" (page 1, lines 49-50) including empirical analysis of gene function (page 1, lines 51-52) as well as developing medicines for diseases and drugs (page 2, lines 1-4). The specification summarizes general sequence uses in modern biotechnology, such as screening assays (page 181, lines 13-34), but never connects the specifically elected sequences (SEQ ID NO: 702, 6223, 10847, and 10848) to any particular or available utility. The above-mentioned list of possible utility for the claimed sequence falls short of a readily available utility. These are non-specific uses that are applicable to many polynucleotides, and are not particular or specific to the primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides being claimed.

Further, these claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides are not supported by a substantial utility, because no substantial utility has been established for the claimed subject matter. SEQ ID NO: 702, 6223, 10847, and 10848 may involved in the predicted protein functions, such as those described in pages 216-241, but the mere fact that these are only "predicted" functions supports the notion that further research would be required to confirm a "real world" context of use. Identifying a sequence itself does not define a "real world" context of use.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Due to a lack of either an art recognized or alleged well established utility, the instant invention has been rejected due to also lacking the required combination of a specific, substantial, and credible utility. Although it may be credible that the polynucleotides involved in the claimed primer sets, polynucleotides, vectors, transformants, oligonucleotides, and antisense polynucleotides may have an important function, the lack of a specific and substantial utility, as explained above, sufficiently supports this rejection.

It is noted that applicant has conducted homology studies (via BLAST, page 2 lines 30-32 and 39-48) to sequences which are known in the prior art and which has a stated sequence similarity or dissimilarity to the claimed sequence to identify predictive functions. Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the

structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular

biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 24-35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

For a sequence putatively assigned a biological function, even if correct, does not appear to be defined as to what use it is to be applied. The significance of the sequence is unconfirmed, further rendering it indiscernible how someone of skill in the art would use such an entity.

Due to the large quantity of experimentation necessary to determine activity or property of the disclosed nucleic acid and recombinant host cell, such that it can be determined how to use the claimed sequence, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, and the breadth of the claims which fail to recite a particular biological activities, the specification fails to teach the skilled artisan how to use the claimed invention.

Also, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to the 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

LACK OF WRITTEN DESCRIPTION

Claims 24-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 702, 6223, 10847, and 10848 which correspond to nucleic acid sequences of isolated cDNA. SEQ ID NO: 702, 6223, 10847, and 10848 and their full length complements meet the written description provisions of 35 U.S.C. 112, first paragraph. However, claims 24-35 are directed to encompass the complements of complements of SEQ ID NO: 702, 6223, 10847, and 10848 as well as a polynucleotide which hybridizes to SEQ ID NO: 10847 which do not meet the written description provision of 35 U.S.C. 112, first paragraph. Due to the unclarity of the claim phrases "comprising *the* nucleotide sequence" (claims 24 and 34), "*the* nucleotide sequence" (claim 28, lines 2, 11-13, and 16-17), "*the* amino acid sequence(s)" (claim 28, lines 5 and 7), "*the* polynucleotide" (claims 24, 27, 28, 30, and 35), and "comprising *the* polynucleotide" (claims 29 and 32), "*the* primer set" (claim 26), and "*the* vector" (claims 31 and 33), "functionally equivalent" (claim 28, lines 9 and 12), "*partial* amino acid sequence" (claim 28, line 14); these claims are directed to encompass polynucleotide sequences that do not meet the written description provision of 35 U.S.C. 112, first paragraph. Claim 28 is directed to encompass a sequence having a recited degree of homology which do not meet the written description provision of 35 U.S.C. 112, first paragraph. Please note the "70% identical" as recited in claim 28 (line 16), could also contain sequences including the entire sequence of SEQ ID NO: 10847 plus up to 30% of additional sequence on either end of SEQ ID NO: 10847 which fails to meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: XXX, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 702, 6223, 10847, and 10848 and their full complement but not the full breadth of claims 24-35 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 24 (line 2), 25 (lines 3 and 5), 34 (line 2) recite the phrase "complementary to" which is vague and indefinite. These claims do not adequately define the phrase which could mean the complementarity is 100%, 90%, or any other degree of similarity. Appropriate definition of the degree of complementarity to the claimed sequences is required. Claims 26, 27, and 29-33 are also rejected due to their direct or indirect dependency from claims 24 and 25.

Claims 24 and 26-35 recite the phrases "comprising *the* nucleotide sequence" (claims 24 and 34), "*the* nucleotide sequence" (claim 28, lines 2, 11-13, and 16-17), "*the* amino acid sequence(s)" (claim 28, lines 5 and 7), "*the* polynucleotide" (claims 24, 27, 28, 30, and 35), and "comprising *the* polynucleotide" (claims 29 and 32), "*the* primer set" (claim 26), and "*the* vector" (claims 31 and 33) which are vague and indefinite. It is unclear if the nucleic acid molecule involved in each of these cases is referring to the entire length of the mentioned nucleotide sequence or just a fragment of the sequence. Clarification of the metes and bounds of these claims via clearer claim wording is requested.

Claim 28 recites the phrase "functionally equivalent" which is vague and indefinite. It is unclear what parameters and to what degree these parameters must be met in order to be

considered "functionally equivalent." Clarification of the metes and bounds of this claim via clearer claim wording is requested. Claims 29-35 are also rejected due to their direct or indirect independence from claim 28.

Claim 28 recites the phrase "*partial* amino acid sequence" which is vague and indefinite. It is unclear how many amino acids must be included to be considered "partial." Clarification of this term is requested via clearer claim wording. Claims 29-35 are also rejected due to their direct or indirect independence from claim 28.

Claim 28 recites the phrase "hybridizes" which is vague and indefinite. It is unclear which criteria the applicants regard as stringent conditions (i.e. buffers, pH of buffer, etc.) or whether low, medium, or high stringency is meant. Applicants can resolve this issue by particularly pointing out the stringent conditions that are intended to allow the cDNA to hybridize. Clarification of the metes and bounds of the instant claim is required. Claims 29-35 are also rejected due to their direct or indirect independence from claim 28.

Claims 34 and 35 recite the phrases "complementary strand thereof" (claim 34) and "portion thereof" (claim 35) which are vague and indefinite. It is unclear what metes and bounds of the "strand" and "portion" are to be considered inclusive in the "thereof" category. Clarification of the metes and bounds of these phrases via clearer claim wording is requested.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 24-27 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Trofatter et al. (P/N 5,707,863).

Due to the unclear claim language "complementary to" (in claims 24, 25, and 34), Trofatter et al. disclose the amplification of cDNA (which inherently contains coding region) and a primer set which comprises an oligo-dT primer (col. 19, lines 49-52) and a 20-mer primer (SEQ ID NO: 13, col. 19, lines 58) which is 65% homologous to a section of the complement of the complementary strand of SEQ ID NO: 702 (residues 208-227). Trofatter et al. disclose a 22-mer primer (SEQ ID NO : 14, col. 19, lines 60-61) which is 36% complementary to SEQ ID NO: 6223 (residues 127-148). Trofatter et al. disclose a cDNA sequence of SEQ ID NO: 15 which the primers of SEQ ID NO: 14 and 13 for residues 315-336 and residues 1189-1208 (of SEQ ID NO: 15) which includes coding region (col. 46-48).

Thus, Trofatter et al. anticipate the limitations of claims 24-27 and 34-35.

Claims 28-35 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Shin et al. (P/N 6,291,645).

As the coding region of SEQ ID NO: 10847 consists of residues 416-1174, Shin et al. disclose a sequence (SEQ ID NO: 8, residues 2599-2620) including a 22-mer which matches residues 767-788 of SEQ ID NO: 10847 in the instant invention, as stated in claim 28. A sequence match printout is enclosed in support of the rejection wherein a continuation parent to Shin et al. is shown to contain the 22-mer sequence match. Shin et al. disclose the sequence of SEQ ID NO: 8 (col. 79-86) encodes an amino acid sequence of a p160 polypeptide (col. 8, lines 51-57). Shin et al. disclose recombinant expression vectors containing nucleic acid molecules of the invention, host cells which contain the recombinant expression vectors, and nucleic acids which are antisense to the nucleic acid molecules described in the invention (abstract and col. 5, lines 24-30).

Thus, Shin et al. anticipate the limitations of claims 28-35.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

April 2, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER